PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : WISNIEWSKI et al. Group Art Unit: 3743

Serial No.: 08/895,936 Examiner : John Ford

Filed : July 17, 1997

For : FREEZING AND THAWING VESSEL WITH THERMAL BRIDGE FORMED BETWEEN HEAT EXCHANGE MEMBERS

Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF RICHARD WISNIEWSKI

1. I am one of the inventors of the above-referenced United States patent application. I am also a named inventor of six U.S. Patents relating to cryopreservation of biopharmaceuticals and numerous pending patent applications. I make the statements herein to the best of my own personal knowledge.

2. I received degrees in Mechanical Engineering and Chemical Engineering from Warsaw Technical University in Warsaw, Poland in 1971. I have over 26 years of experience in applied research, process and product development, process control, equipment and device design, industrial facility design and project and team management in the biopharmaceutical field.

3. I am a co-founder and currently the Chief Technology Officer of Integrated Biosystems, Inc.

4. Prior to my current position, I have held senior engineering and management positions with Wyeth-Ayerst, Genentech, Inc., Bepex Corporation and Ares Serono. While at

Genentech, Inc., I was a Principal Process Engineer responsible for pioneering work in the design of equipment and processes for biopharmaceutical manufacturing, including systems for cryopreservation, chromatography, filtration and bioreactors and aseptic processing used in large scale production.

5. I have published numerous articles in the areas of cryobiology and cryopreservation. While I was working for Genentech, Inc., I co-published, with Vincent L. Wu, an article entitled "Large-Scale Freezing and Thawing of Biopharmaceutical Drug Product" for the Advanced Technologies For Manufacturing Of Aseptic & Terminally Sterilized Pharmaceuticals & Biopharmaceuticals convention during the Proceedings of the International Congress in 1992 ("the 1992 article"). I have provided a copy of this article in Exhibit A. This 1992 article is similar to the 1996 article previously disclosed to the Patent Office during the prosecution of the above-reference application.

6. The 1992 article discloses a freeze-thaw vessel for biopharmaceutical products having an internal heat transfer coil with fins welded to the external surface of the coil pipe which I designed. The figure on page 134 of the article accurately depicts the heat transfer coil and fin arrangement within the vessel. This article does not disclose or suggest the formation of a thermal transfer bridge, as defined in the above-reference application, by the medium in a gap between the fins and the interior wall of the vessel, even after the medium in the gap is frozen.

7. In Exhibit B, I have provided a schematic representation of the freezing which would have occurred in the vessel disolosed in the 1992 article at a period in time before the medium between the fin and the interior wall of the vessel is frozen along with a graph showing the temperature distribution along the radius of the vessel. Exhibit B depicts a schematic sectional view of the interior of the vessel disclosed in the 1992 article. To the best of my knowledge the temperature graph reasonably resembles the temperature profile along the line (R-R) at different points. For example, at the center of the pipe within the fin the temperature is Tc. while the temperature at the edge of the fin is Tft. As shown in

this graph, the temperature in the gap between the fin and the interior wall increases and then decreases from the distal end of the fin to the interior wall. This temperature distribution occurs because the gap between the distal end of the fin and interior wall is too large. Accordingly, no thermal bridge is formed because heat is not transferred from the fin through the medium in the gap to the interior wall. Rather, heat is transferred from a location in the gap between the fin and the interior wall to both the fin and the interior wall.

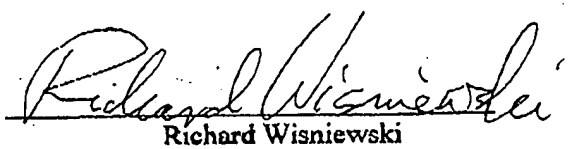
8. In Exhibit C, I have provided a similar schematic view of the same vessel. However, the freezing is at a period in time when the frozen medium built up on the fin meets the frozen medium built up on the interior wall. To the best of my knowledge the temperature graph reasonably resembles the temperature distribution along the line (R-R) at different points. As shown in this graph, the temperature in the gap between the fin and the interior wall increases and then decreases from the distal end of the fin to the interior wall. This temperature distribution occurs because the gap between the distal end of the fin and interior wall is too large. Accordingly, no thermal bridge is formed because heat is not transferred from the fin through the medium in the gap to the interior wall. Rather, heat is transferred from a point in the gap between the fin and the interior wall to both the fin and the interior wall.

9. In Exhibit D, I have provided a similar schematic view of the same vessel. However, the freezing is at a period in time when the medium in the gap between the fin and the interior wall is completely frozen. To the best of my knowledge the temperature graph reasonably resembles the temperature distribution along the line (R-R) at different points. As shown in this graph, the temperature in the gap between the fin and the interior wall increases and then decreases from the distal end of the fin to the interior wall, even when the medium is frozen. This temperature distribution occurs because the gap between the distal end of the fin and interior wall is too large. Accordingly, no thermal bridge is formed, even after the medium in the gap is frozen, because heat is not transferred from the fin through the medium in the gap to the interior wall. Furthermore, even after

additional freezing may occur, including total freezing within the vessel, no thermal bridge is formed in the gap area. Rather, heat is transferred from a point in the gap between the fin and the interior wall to both the fin and the interior wall.

10. With respect to the above-referenced application, a thermal bridge will not form if the gap between the heat transfer members and the interior wall of the vessel is too large, even after the medium in the gap is frozen. If this gap is too large, heat would be transferred from a location within the gap to both the heat transfer member and the interior wall similar to the Genentech device, not from the heat transfer member to the interior wall as required by the formation of a thermal bridge.

11. I declare under penalty of perjury under the laws of the United States of America that the foregoing information contained in this Affidavit is true and correct.

January _23__, 2002 

Richard Wisniewski